

What is claimed is:

1. A method for screening a plurality of compounds so as to identify at least one compound exhibiting cognitive enhancing activity, comprising:

- a) determining *in vitro* efficacy and  $EC_{50}$  values for each compound at an  $\alpha_1\beta_2\gamma_2$  or an  $\alpha_5\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor;
- b) determining an *in vitro* efficacy value for each compound at a GABA<sub>A</sub> receptor comprising an  $\alpha_2$  or  $\alpha_3$  subunit; and
- c) identifying as exhibiting cognitive enhancing activity a compound having: an  $EC_{50}$  value determined in a) of less than about 200nM, an efficacy value determined in a) of less than about -5%, and an efficacy value determined in b) of greater than about 5%.

2. The method of Claim 1 wherein the  $EC_{50}$  measured in step a) is less than 150 nM.

3. The method of Claim 2 wherein the *in vitro* efficacy measured at said  $\alpha_1\beta_2\gamma_2$  GABA<sub>A</sub> subtype receptor or said  $\alpha_5\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor is less than -10%.

4. The method of Claim 3 wherein the *in vitro* efficacy measured at said GABA<sub>A</sub> receptor comprised of said  $\alpha_2$  subunit or said  $\alpha_3$  subunit is greater than 10%.

5. The method of Claim 1 wherein the *in vitro* efficacy measured at said  $\alpha_1\beta_2\gamma_2$  GABA<sub>A</sub> subtype receptor or said  $\alpha_5\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor is less than -10%.

5 6. The method of Claim 5 wherein the *in vitro* efficacy measured at said GABA<sub>A</sub> receptor comprised of said  $\alpha_2$  or said  $\alpha_3$  subunit is greater than 10%.

10 7. The method of Claim 1 wherein the GABA<sub>A</sub> receptor comprised of said  $\alpha_2$  subunit is an  $\alpha_2\beta_3\gamma_2$  GABA<sub>A</sub> receptor or the GABA<sub>A</sub> receptor comprised of said  $\alpha_3$  subunit is an  $\alpha_3\beta_3\gamma_2$  GABA<sub>A</sub> receptor.

15 8. A method for screening compounds for cognitive enhancing activity, comprising:

- 20 a) selecting compounds having a binding affinity less than 100 nM at any GABA<sub>A</sub> receptor;
- b) determining *in vitro* efficacy and EC<sub>50</sub> values for each selected compound at an  $\alpha_1\beta_2\gamma_2$  or  $\alpha_5\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor;
- 25 c) determining *in vitro* efficacy and EC<sub>50</sub> values for each selected compound at a GABA<sub>A</sub> receptor comprised of an  $\alpha_2$  or  $\alpha_3$  subunit; and
- d) identifying as having cognitive enhancing activity any compound having an EC<sub>50</sub> value determined in b) of less than 200nM and an efficacy value measured in b) of less than -5%, and an efficacy value measured in c) of greater than 5%.

9. A method of providing a pharmaceutical preparation to patients in need of cognition enhancing treatment comprising:

- 5 a) obtaining at least one compound identified as exhibiting cognition enhancing activity by the method of Claim 1;
- b) testing said at least one compound and submitting results of said testing as part of submission of information under a United States Federal law which regulates the manufacture, use, or sale of drugs or
- 10 veterinary products;
- c) showing a pharmaceutical preparation comprising said at least one compound to be safe for use as required by the provisions of the Federal Food Drug And Cosmetic Act; and
- 15 d) offering the pharmaceutical preparation for sale in the United States of America for use as a cognition enhancing drug or cognition enhancing veterinary product.

20 10. A method for screening a plurality of compounds for cognitive enhancing activity, comprising:

- a) determining *in vitro* efficacy and  $EC_{50}$  values for each compound at  $\alpha_1\beta_2\gamma_2$  or  $\alpha_5\beta_3\gamma_2$  GABA<sub>A</sub> receptors;
- b) determining *in vitro* efficacy for each compound at a
- 25 GABA<sub>A</sub> receptor comprised of an  $\alpha_2$  or  $\alpha_3$  subunit;
- c) determining the *in vivo* effect of each compound in an animal model for measuring cognitive enhancement;
- d) determining the *in vivo* effects of each compound in an animal model for proconvulsant activity by measuring
- 30 a seizure threshold in the presence of a seizure inducing compound or in an animal model that predicts anxiogenic effects; and

e) identifying a cognitive enhancing compound as a compound having cognitive enhancing properties when the  $EC_{50}$  measured in step a) is less than 200nM and the efficacy measured in step a) is less than -5% and the efficacy measured in step b) is greater than 5% and said compound produces a statistically significant ( $p < 0.05$ ) positive effect in the animal model indicative of cognitive enhancement and said compound does not produce an effect in the animal model predictive of proconvulsant activity of more than a 25% decrease in the seizure threshold in the presence of the seizure inducing drug, or does not produce a change that is statistically significant in said model, or the compound does not produce a statistically significant effect in the animal model that predicts anxiogenic effects.

11. A method for screening compounds for cognitive enhancing properties, comprising:

- a) selecting compounds having binding affinities of less than 100 nM at any  $GABA_A$  receptor;
- b) measuring the *in vitro* efficacy of each compound at an  $\alpha_1\beta_2\gamma_2$  or  $\alpha_5\beta_3\gamma_2$   $GABA_A$  receptor;
- c) measuring the *in vitro* efficacy of each compound at a  $GABA_A$  receptor comprised of an  $\alpha_2$  or  $\alpha_3$  subunit;
- d) measuring the *in vivo* effect of each compound in an animal model predictive of cognitive enhancement;
- e) measuring the *in vivo* side effects of each compound in an animal model that predicts proconvulsant activity by measuring a seizure threshold in the presence of a seizure inducing compound or measuring the *in vivo* side

effects of each compound in an animal model that predicts anxiogenic effects; and

f) identifying as a cognitive enhancing compound a particular compound for which the  $EC_{50}$  measured in step b) is less than 200nM and the efficacy measured in step b) is less than -5% and the efficacy measured in step c) is greater than 5% and said particular compound produces a statistically significant ( $p < 0.05$ ) positive effect in the animal model indicative of cognitive enhancement and said particular compound does not produce an effect in the animal model predictive of proconvulsant activity of more than a 25% decrease in the seizure threshold in the presence of the seizure inducing drug, or does not produce a change that is statistically significant in said model, or said particular compound does not produce a statistically significant effect in the animal model that predicts anxiogenic effects.

12. A method for screening compounds for hypnotic activity, comprising:

- a) determining  $EC_{50}$  and *in vitro* efficacy of each compound at an  $\alpha_2\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor or an  $\alpha_3\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor;
- b) determining *in vitro* efficacy of each compound at a GABA<sub>A</sub> receptor comprised of an  $\alpha_1$  or  $\alpha_5$  subunit; and
- c) selecting a compound having an  $EC_{50}$  determined in a) of less than 200nM, an *in vitro* efficacy determined in

a) of greater than 10% for said  $\alpha_2\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor or greater than 50% for said  $\alpha_3\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor; and an *in vitro* efficacy value determined in b) of less than 50% for the GABA<sub>A</sub> receptor comprised of an  $\alpha_1$  subunit or less than 45% for the GABA<sub>A</sub> receptor comprised of an  $\alpha_5$  subunit.

13. The method of Claim 12 wherein the *in vitro* efficacy value measured at said  $\alpha_2\beta_3\gamma_2$  receptor is greater than 20% or the *in vitro* efficacy value measured said  $\alpha_3\beta_3\gamma_2$  GABA<sub>A</sub> receptor is greater than 60%.

14. The method of Claim 13 wherein the *in vitro* efficacy value measured at the GABA<sub>A</sub> receptor comprised of said  $\alpha_1$  subunit is less than 45% or the *in vitro* efficacy value measured at the GABA<sub>A</sub> receptor comprised of said  $\alpha_5$  subunit is less than 40%.

15. The method of Claim 12 wherein the *in vitro* efficacy value measured at the GABA<sub>A</sub> receptor comprised of said  $\alpha_1$  subunit is less than 45% or the *in vitro* efficacy value measured at the GABA<sub>A</sub> receptor comprised of said  $\alpha_5$  subunit is less than 40%.

16. The method of Claim 12 wherein the  $EC_{50}$  measured at said  $\alpha_2\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor or at said  $\alpha_3\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor is less than 150 nM.

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17. The method of Claim 16 wherein the *in vitro* efficacy measured at said  $\alpha_2\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor is greater than 20% or the *in vitro* efficacy measured at said  $\alpha_3\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor is greater than 60%.

18. The method of Claim 17 wherein the *in vitro* efficacy measured at the GABA<sub>A</sub> receptor comprised of said  $\alpha_1$  subunit is less than 45% or the *in vitro* efficacy measured at the GABA<sub>A</sub> receptor comprised of said  $\alpha_5$  subunit is less than 40%.

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19. The method of Claim 16 wherein the *in vitro* efficacy measured at the GABA<sub>A</sub> receptor comprised of said  $\alpha_1$  subunit is less than 45% or the *in vitro* efficacy measured at the GABA<sub>A</sub> receptor comprised of said  $\alpha_5$  subunit is less than 40%.

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20. The method of Claim 12 wherein the GABA<sub>A</sub> receptor comprised of an  $\alpha_1$  subunit is an  $\alpha_1\beta_2\gamma_2$  GABA<sub>A</sub> subtype receptor

or the GABA<sub>A</sub> receptor comprised of an  $\alpha_5$  subunit is an  $\alpha_5\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor.

21. A method for screening a plurality of compounds so as to identify at least one compound exhibiting hypnotic activity, comprising:

- a) selecting a plurality of compounds having a binding affinity of less than 100 nM at any GABA<sub>A</sub> receptor.
- b) determining EC<sub>50</sub> and *in vitro* efficacy values for each selected compound at an  $\alpha_2\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor or at an  $\alpha_3\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor;
- c) determining *in vitro* efficacy values for each selected compound at a GABA<sub>A</sub> receptor comprised of an  $\alpha_1$  or an  $\alpha_5$  subunit; and
- d) identifying as exhibiting hypnotic activity each selected compound having an EC<sub>50</sub> value determined in b) of less than 200nM, an *in vitro* efficacy value measured in b) of greater than 10% for said  $\alpha_2\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor or greater than 50% for said  $\alpha_3\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor, and an *in vitro* efficacy value determined in c) of less than 50% for the GABA<sub>A</sub> receptor comprised of said  $\alpha_1$  subunit or less than 45% for the GABA<sub>A</sub> receptor comprised of said  $\alpha_5$  subunit.



22. A method for screening a plurality of compounds so as to identify compounds exhibiting hypnotic activity, comprising:

- a) measuring the  $EC_{50}$  and *in vitro* efficacy of each compound at an  $\alpha_2\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor or an  $\alpha_3\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor;
- b) measuring the *in vitro* efficacy of each compound at a GABA<sub>A</sub> receptor comprised of an  $\alpha_1$  or  $\alpha_5$  subunit; and
- c) measuring the *in vivo* effect of each compound in an animal model indicative of hypnotic effects;
- d) measuring the *in vivo* effect of each compound in an animal model indicative of cognitive impairment; and
- e) identifying a compound as having hypnotic activity when the  $EC_{50}$  measured in step a) is less than 200nM, the *in vitro* efficacy measured in step a) is greater than 10% for said  $\alpha_2\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor or greater than 50% for said  $\alpha_3\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor, and the *in vitro* efficacy measured in step b) is less than 50% for the GABA<sub>A</sub> receptor comprised of said  $\alpha_1$  subunit or less than 45% for the GABA<sub>A</sub> receptor comprised of said  $\alpha_5$  subunit and said compound produces a statistically significant ( $p < 0.05$ ) positive effect

in the animal model indicative of sedation and said compound does not produce a statistically significant effect in the animal model indicative of cognitive impairment.

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23. A method for screening a plurality of compounds so as to identify at least one compound exhibiting hypnotic activity, comprising:

a) selecting compounds having a binding affinity less than 100 nM at any GABA<sub>A</sub> receptor;

b) measuring the EC<sub>50</sub> and *in vitro* efficacy of each selected compound at an  $\alpha_2\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor or an  $\alpha_3\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor;

c) measuring the *in vitro* efficacy of each selected compound at a GABA<sub>A</sub> receptor comprised of an  $\alpha_1$  or  $\alpha_5$  subunit; and

d) measuring the *in vivo* effect of each selected compound in an animal model indicative of sedative effects;

e) measuring the *in vivo* effect of each selected compound in an animal model indicative of cognitive impairment; and

f) identifying as having hypnotic activity each selected compound for which the EC<sub>50</sub> measured in step

b) is less than 200nM, the *in vitro* efficacy measured in step b) is greater than 10% for said  $\alpha_2\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor or greater than 50% for said  $\alpha_3\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor, and the *in vitro* efficacy measured in step c) is less than 50% for the GABA<sub>A</sub> receptor comprised of said  $\alpha_1$  subunit or less than 45% for the GABA<sub>A</sub> receptor comprised of said  $\alpha_5$  subunit and said compound produces a statistically significant ( $p < 0.05$ ) positive effect in the animal model indicative of hypnotic effects and said compound does not produce a statistically significant effect in the animal model indicative of cognitive impairment.

24. A method for screening a plurality of compounds so as to identify compounds exhibiting anxiolytic activity, comprising:

- a) determining *in vitro* efficacy and EC<sub>50</sub> value for each compound at an  $\alpha_2\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor or an  $\alpha_3\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor;
- b) determining *in vitro* efficacy values for each compound at a GABA<sub>A</sub> receptor comprised of an  $\alpha_1$  subunit or an  $\alpha_5$  subunit; and

c) identifying as exhibiting anxiolytic activity each compound having an  $EC_{50}$  value determined in a) of less than 200nM and an efficacy value measured in a) greater than the efficacy measured in b).

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25. The method of Claim 24 wherein the  $EC_{50}$  measured in step a) is less than 150 nM.

26. The method of Claim 25 wherein the *in vitro* efficacy measured at said  $\alpha_2\beta_3\gamma_2$  or said  $\alpha_3\beta_3\gamma_2$  GABA<sub>A</sub> receptor is greater than 20%.

27. The method of Claim 25 wherein the *in vitro* efficacy measured at said  $\alpha_2\beta_3\gamma_2$  or said  $\alpha_3\beta_3\gamma_2$  GABA<sub>A</sub> receptor is greater than 30%.

28. The method of Claim 27 wherein the *in vitro* efficacy measured at said GABA<sub>A</sub> receptor comprised of said  $\alpha_1$  or said  $\alpha_5$  subunit is less than 20%.

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29. The method of Claim 24 wherein the *in vitro* efficacy measured at said  $\alpha_2\beta_3\gamma_2$  or  $\alpha_3\beta_3\gamma_2$  GABA<sub>A</sub> receptor is greater than 20%.

30. The method of Claim 24 wherein the *in vitro* efficacy measured at said  $\alpha_2\beta_3\gamma_2$  or  $\alpha_3\beta_3\gamma_2$  GABA<sub>A</sub> receptor is greater than 30%.

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31. The method of Claim 30 wherein the *in vitro* efficacy measured at said GABA<sub>A</sub> receptor comprised of said  $\alpha_1$  or said  $\alpha_5$  subunit is less than 20%.

32. The method of Claim 24 wherein the GABA<sub>A</sub> receptor comprised of said  $\alpha_1$  subunit is an  $\alpha_1\beta_2\gamma_2$  GABA<sub>A</sub> subtype receptor or the GABA<sub>A</sub> receptor comprised of said  $\alpha_5$  subunit is an  $\alpha_5\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor.

33. A method for screening for compounds having anxiolytic activity, comprising:

a) selecting a compound having a binding affinity less than 100 nM at any GABA<sub>A</sub> receptor;

b) measuring *in vitro* efficacy and EC<sub>50</sub> values for each compound at an  $\alpha_2\beta_3\gamma_2$  or  $\alpha_3\beta_3\gamma_2$  GABA<sub>A</sub> receptor;

c) measuring *in vitro* efficacy values for each compound at a GABA<sub>A</sub> receptor comprised of an  $\alpha_1$  or  $\alpha_5$  subunit;

and

d) selecting a compound having an  $EC_{50}$  value measured in a) of less than 200nM and an efficacy value measured in b) greater than the efficacy measured in c).

5 34. A method for screening compounds so as to select at least one compound having anxiolytic activity, comprising:

10 a) measuring *in vitro* efficacy for each compound at an  $\alpha_2\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor or an  $\alpha_3\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor;

15 b) measuring *in vitro* efficacy and  $EC_{50}$  values for each compound at a GABA<sub>A</sub> receptor comprised of an  $\alpha_1$  or  $\alpha_5$  subunit;

c) measuring *in vivo* effects of each compound in an animal model indicative of anxiolytic activity;

d) measuring *in vivo* effects of each compound in an animal model indicative of sedative effects; and

20 e) selecting each compound having: an  $EC_{50}$  value measured in a) of less than 200nM, an efficacy value measured in b) greater than the efficacy measured in step c), a statistically significant ( $p < 0.05$ ) positive effect in the animal model indicative of anxiolytic activity, and no statistically significant effect in the animal indicative of sedative effects.

35. A method for screening a plurality of compounds so as to identify at least one compound having anxiolytic activity, comprising:

- a) selecting a compound having a binding affinity less than 100 nM at any GABA<sub>A</sub> receptor;
- b) measuring *in vitro* efficacy and EC<sub>50</sub> values for each selected compound at an  $\alpha_2\beta_3\gamma_2$  or  $\alpha_3\beta_3\gamma_2$  GABA<sub>A</sub> receptor;
- c) measuring *in vitro* efficacy for each selected compound at a GABA<sub>A</sub> receptor comprised of an  $\alpha_1$  or  $\alpha_5$  subunit;
- d) measuring *in vivo* effects of each selected compound in an animal model indicative of anxiolytic activity;
- e) measuring *in vivo* effect of each selected compound in an animal model indicative of sedative effects; and
- f) selecting a compound having: an EC<sub>50</sub> value measured in b) of less than 200nM, an efficacy measured in c) greater than the efficacy measured in d), a statistically significant ( $p < 0.05$ ) positive effect in the animal model indicative of anxiolytic activity, and no statistically significant effect in the animal indicative of sedative effects.

36. A method for screening a plurality of compounds so as to identify compounds exhibiting antidepressant activity, comprising:

- a) determining *in vitro* efficacy and EC<sub>50</sub> values for each compound using an  $\alpha_2\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor or an  $\alpha_3\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor;
- b) determining *in vitro* efficacy values for each compound at a GABA<sub>A</sub> receptor comprised of an  $\alpha_1$  or an  $\alpha_5$  subunit; and
- c) identifying as having antidepressant activity a compound having an EC<sub>50</sub> value determined in a) of less than 200nM and an efficacy value determined in a) of greater than the efficacy value determined in b).

37. The method of Claim 36 wherein the EC<sub>50</sub> value determined using said  $\alpha_2\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor or said  $\alpha_3\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor is less than 150 nM.

38. The method of Claim 37 wherein the *in vitro* efficacy measured at said  $\alpha_2\beta_3\gamma_2$  or said  $\alpha_3\beta_3\gamma_2$  GABA<sub>A</sub> receptor is greater than 20%.



39. The method of Claim 37 wherein the *in vitro* efficacy measured at said  $\alpha_2\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor or said  $\alpha_3\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor is greater than 30%.

5 40. The method of Claim 39 wherein the *in vitro* efficacy measured at said GABA<sub>A</sub> receptor comprised of said  $\alpha_1$  subunit or said  $\alpha_5$  subunit is less than 20%.

10 41. The method of Claim 36 wherein the *in vitro* efficacy measured at said  $\alpha_2\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor or said  $\alpha_3\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor is greater than 20%.

15 42. The method of Claim 36 wherein the *in vitro* efficacy measured at said  $\alpha_2\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor or said  $\alpha_3\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor is greater than 30%.

43. The method of Claim 42 wherein the *in vitro* efficacy measured at said GABA<sub>A</sub> receptor comprised of said  $\alpha_1$  subunit or said  $\alpha_5$  subunit is less than 20%.

20 44. The method of Claim 36 wherein the GABA<sub>A</sub> receptor comprised of said  $\alpha_1$  subunit is an  $\alpha_1\beta_2\gamma_2$  GABA<sub>A</sub> subtype

receptor or the GABA<sub>A</sub> receptor comprised of said  $\alpha_5$  subunit  
is an  $\alpha_5\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor.

45. A method for screening compounds for antidepressant  
activity, comprising:

- a) selecting compounds having a binding affinity less than 100 nM at any GABA<sub>A</sub> receptor;
- b) determining *in vitro* efficacy and EC<sub>50</sub> values for the selected compounds using an  $\alpha_2\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor or an  $\alpha_3\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor;
- c) determining *in vitro* efficacy for the selected compounds using a GABA<sub>A</sub> receptor comprised of an  $\alpha_1$  or an  $\alpha_5$  subunit; and
- d) identifying as having antidepressant activity a compound having an EC<sub>50</sub> as determined in b) of less than 200nM and an efficacy value as determined in b) greater than the efficacy value determined in c).

46. A method for screening compounds for antidepressant  
activity, comprising:

- a) determining *in vitro* efficacy and EC<sub>50</sub> values for each compound using an  $\alpha_2\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor or  $\alpha_3\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor;

b) determining *in vitro* efficacy values for each compound at a GABA<sub>A</sub> receptor comprised of an  $\alpha_1$  or an  $\alpha_5$  subunit;

c) determining *in vivo* effect of said compound in an animal model indicative of antidepressant activity;

d) determining the *in vivo* effect of said compound in an animal model indicative of sedative effects; and

e) identifying as an antidepressant a compound that produces an EC<sub>50</sub> value as determined in a) of less than 200nM, and an efficacy value as determined in b) greater than the efficacy value from c), and (i) produces a statistically significant ( $p < 0.05$ ) positive effect in the animal model indicative of antidepressant activity and (ii) does not produce a statistically significant effect in the animal model indicative of sedative effects.

47. A method for screening compounds for antidepressant activity, comprising:

a) selecting test compounds having a binding affinity less than 100 nM at any GABA<sub>A</sub> receptor;

b) determining *in vitro* efficacy and EC<sub>50</sub> value for each test compound using an  $\alpha_2\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor or an  $\alpha_3\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor;

c) determining *in vitro* efficacy value for each test compound at a GABA<sub>A</sub> receptor comprised of an  $\alpha_1$  subunit or an  $\alpha_5$  subunit;

d) determining the *in vivo* effect of each test compound in an animal model indicative of antidepressant activity;

e) determining the *in vivo* effect of each test compound in an animal model indicative of sedative effects; and

f) identifying as an antidepressant a compound that produces: an EC<sub>50</sub> value as determined in b) of less than 200nM, an efficacy value as determined in c) greater than the efficacy value from d), and (i) produces a statistically significant ( $p < 0.05$ ) positive effect in the animal model indicative of antidepressant activity and (ii) does not produce a statistically significant effect in the animal model indicative of sedative effects.

48. A method of providing pharmaceutical compounds to patients in need of hypnotic treatment comprising:

- a) obtaining at least one compound identified as exhibiting hypnotic activity by the method of Claim 21;
- b) testing said at least one compound and submitting results of said testing as part of submission of

information under a United States Federal law which regulates the manufacture, use, or sale of drugs or veterinary products

c) showing a pharmaceutical preparation comprising said at least one compound to be safe for use as required by the provisions of the Federal Food Drug And Cosmetic Act; and

d) offering the pharmaceutical preparation for sale in the United States of America for use as an hypnotic drug or hypnotic veterinary product.

49. A method of providing a pharmaceutical preparation to patients in need of anxiolytic treatment comprising:

a) obtaining at least one compound identified as exhibiting anxiolytic activity by the method of Claim 24;

b) submitting information regarding the anxiolytic activity of said at least one compound as part of an application under a United States Federal law which regulates the manufacture, use, or sale of drugs or veterinary products

c) showing a pharmaceutical preparation comprising said at least one compound to be safe for use as required by

the provisions of the Federal Food Drug And Cosmetic Act; and

d) offering the pharmaceutical preparation for sale in the United States of America for use as an anxiolytic drug or anxiolytic veterinary product.

50. A method of providing a pharmaceutical preparation to patients in need of antidepressant treatment comprising:

- a) obtaining at least one compound identified as exhibiting antidepressant activity by the method of Claim 36;
- b) testing said at least one compound and submitting results of said testing as part of submission of information under a United States Federal law which regulates the manufacture, use, or sale of drugs or veterinary products
- c) showing a pharmaceutical preparation comprising said at least one compound to be safe for use as required by the provisions of the Federal Food Drug And Cosmetic Act; and
- d) offering the pharmaceutical preparation for sale in the United States of America for use as an antidepressant drug or antidepressant veterinary product.